EXHIBIT F

CAHILL GORDON & REINDEL LLP
EIGHTY PINE STREET
NEW YORK, NY 10005-1702

FLOYD ABRAMS
L. HOWARD ADAMS
ROBERT A. ALESSI
HELENE R. BANKS
ANIRUDH BANSAL
DAVID L. BARASH
LANDIS C. BEST
BRADLEY J. BONDI
SUSAN BUCKLEY
KEVIN J. BURKE
JAMES J. CLARK
BENJAMIN J. COHEN
SEAN M. DAVIS
STUART G. DOWNING
ADAM M. DWORKIN
ANASTASIA EFIMOVA
JENNIFER B. EZRING
JOAN MURTAGH FRANKEL
JONATHAN J. FRANKEL

BART FRIEDMAN
PIERRE M. GENTIN
CHARLES A. GILMAN
JASON M. HALL
WILLIAM M. HARTNETT
CRAIG M. HOROWITZ
DOUGLAS S. HOROWITZ
TIMOTHY B. HOWELL
DAVID G. JANUSZEWSKI
ELAI KATZ
THOMAS J. KAVALER
BRIAN S. KELLEHER
DAVID N. KELLEY
RICHARD KELLY
CHÉRIE R. KISER*
EDWARD P. KRUGMAN
JOEL KURTZBERG
TED B. LACEY
MARC R. LASHBROOK

TELEPHONE: (212) 701-3000
WWW.CAHILL.COM

1990 K STREET, N.W.
WASHINGTON, DC 20006-1181
(202) 862-8900

CAHILL GORDON & REINDEL (UK) LLP
24 MONUMENT STREET
LONDON EC3R 8AJ
+44 (0)20 7920 9800

WRITER'S DIRECT NUMBER

(212) 701-3041

ALIZA R. LEVINE
JOEL H. LEVITIN
GEOFFREY E. LIEBMANN
ANN S. MAKICH
JONATHAN I. MARK
BRIAN T. MARKLEY
WILLIAM J. MILLER
NOAH B. NEWITZ
MICHAEL J. OHLER
DAVID R. OWEN
JOHN PAPACHRISTOS
LUIS R. PENALVER
KIMBERLY PETILLO-DÉCOSSARD
MICHAEL W. REDDY
OLEG REZZY
JAMES ROBINSON
THORN ROSENTHAL
TAMMY L. ROY

JONATHAN A. SCHAFFZIN
JOHN SCHUSTER
MICHAEL A. SHERMAN
DARREN SILVER
JOSIAH M. SLOTNICK
RICHARD A. STIEGLITZ JR.
SUSANNA M. SUH
ANTHONY K. TAMA
JONATHAN D. THIER
JOHN A. TRIPODORO
GLENN J. WALDRIP, JR.
HERBERT S. WASHER
MICHAEL B. WEISS
S. PENNY WINDLE
DAVID WISHENGRAD
COREY WRIGHT
JOSHUA M. ZELIG
DANIEL J. ZUBKOFF

*ADMITTED IN DC ONLY

December 15, 2016

Re: Request #2 Pursuant to Sections 4.2(f) and 5.4(b) of the CVR Agreement – Sanofi's Diligent Efforts

Dear Sir/Madam:

Reference is made to the Contingent Value Rights Agreement, dated March 30, 2011, by and between Sanofi-Aventis ("Sanofi") and UMB Bank, N.A. ("Trustee"), as successor to American Stock Transfer & Trust Company LLC (the "CVR Agreement").[1]

This Firm represents the Trustee in the litigation captioned UMB Bank N.A. v. Sanofi, currently pending in the Southern District of New York (the "Sanofi Action"). At issue in that litigation is, *inter alia*, the issue of Sanofi's Diligent Efforts, or lack thereof, to achieve the Approval Milestone and Product Sales Milestone #1.

The CVR Agreement contemplates the payment of up to four Product Sales Milestones. CVR Agreement at § 3.1. The Trustee has charged this Firm with investigating whether Sanofi is currently discharging its obligation to "use Diligent Efforts to achieve . . . the [other] Product Sales Milestones." CVR Agreement at § 7.10. Section 4.2(f) provides that the Trustee is "entitled to examine the books, records and premises of [Sanofi] . . . at the sole cost of the Company." Furthermore, Section 5.4(b) provides that Sanofi must "file with the Trustee such additional information, documents and reports with respect to compliance by the Company with the conditions and covenants of this CVR Agreement as may be required from time to time by the Trustee."

Therefore, pursuant to Section 4.2(f) and 5.4(b) thereof, we request that Sanofi file and/or make available, as applicable, the books, records, premises, information, documents and reports specified below. Please also confirm that Sanofi agrees to reimburse the Trustee for any costs (including those of this Firm) and expenses incurred in connection with such examination as required by Section 4.2(f) of the CVR Agreement.

---

[1] Unless otherwise defined in this letter, capitalized terms shall be as set forth in the CVR Agreement.

There are developments in the competitive environment relating to the treatment of multiple sclerosis that, because of the delay in the approval and launch of Lemtrada, have exacerbated the risk that Sanofi may not timely achieve any of the Product Milestones.[2] The Trustee is investigating whether Sanofi should immediately undertake commercial and development activities to improve the probability that Product Sales Milestones #2 through 4 will be timely achieved. The documents requested below are sought to aid the Trustee's investigation of whether Sanofi's prior actions and/or current efforts are in compliance with the standard of performance required by the CVR Agreement. The Trustee's specific requests are set forth below.

I. Clinical Development Activity to Reduce or Prevent Secondary Autoimmunity

Lemtrada has long been recognized as a path-breaking approach to the treatment of autoimmune disease, including multiple sclerosis. Its assumed mechanism of action, the breaking of tolerance, implies that it always had the potential to be a cure for such diseases. As Mr. Viehbacher noted in 2011, patients treated with Lemtrada in the Phase II clinical trial were disease-free for five years and, therefore, Lemtrada "is about as close to a cure as you are going to come." May 9, 2011 Transcript. The Phase III data, as well as data from the extension and tracking trials using Lemtrada, according to Sanofi executives, supports this view. See February 11, 2016 Transcript (comments of David Meeker, Executive Vice President, Sanofi Specialty Care); October 29, 2015 Transcript (comments of Olivier Brandicourt, CEO, Sanofi SA); see also September 16, 2016 Press Release (noting treatment effects maintained over six years with Lemtrada). It is surprising, therefore, that Lemtrada sales have been, by most measures, disappointing.

One of the reasons that Lemtrada is not prescribed more frequently is the perception that its administration can result in serious adverse events (each an "SAE"). Of particular concern are autoimmune responses involving the thyroid, such as immune thrombocytopenic purpura and Goodpasture syndrome.[3] While the thyroid disorders are variable, ranging from transient abnormalities to severe Graves' hyperthyroidism, the FDA clearly considered the SAE profile of Lemtrada to be high relative to its perceived efficacy.[4] As a result, the FDA required a "black box warning" for Lemtrada, which is generally known to reduce the number of prescriptions written.

---

[2] For example, the potential launch of ocrelizumab by early 2017 mandates that Sanofi accelerate its Diligent Efforts to achieve the Product Sales Milestones.

[3] Autoimmunity refers to a condition where the body no longer can distinguish itself from foreign antigens or pathogens. Multiple sclerosis is an example of an autoimmune condition. Autoimmunity can present in different ways. In the case of Lemtrada-induced autoimmunity, it is often manifested by a decrease in thyroid function; the thyroid being an organ closely involved in immune regulation. G. Daniels, et al., "Alemtuzumab-Related Thyroid Dysfunction in a Phase 2 Trial of Patients With Relapsing-Remitting Multiple Sclerosis," 99 J. CLIN. ENDO. & METABOLISM 2013 (Oct. 2013).

[4] This letter is not the appropriate forum to address the open issue of whether, *inter alia*, during the negotiation of the label for Lemtrada, Sanofi, either because it should have conducted the clinical investigations suggested in this letter or because of better advocacy relating to the risk/benefit ratio of the Product, could have avoided or ameliorated the impact of the "black box warning." We note, for example, that Gilenya (fingolimod) has no black box warning.

However, our review of the medical literature suggests that these risks are either overstated or, more importantly, can be ameliorated by additional clinical research by Sanofi.[5]

The current scientific view is that the autoimmunity occurring after Lemtrada therapy for multiple sclerosis is caused by reconstitution of the immune system upon cessation of treatment.[6] Lemtrada works, in part, because it depletes B and T cells, essential components of the immune response that cause the initial autoimmune disease to be treated in the first place. In an apparent paradox,[7] upon cessation of treatment, the previously-suppressed immune response returns. However, because of an imbalance in the rate at which the B and T-cells return, the body is attacked by its own immune response;[8] that is, immune reactive B cells appear to recover at a faster rate than immune regulatory T cells, resulting in a disorderly immune response. Given the presumed mechanism of action of reconstitution autoimmunity after Lemtrada treatment, as noted below, there are numerous clinical approaches that could be fruitful.[9]

The Trustee's inquiry is not idle curiosity. Even before the initiation of controlled clinical trials of Lemtrada for multiple sclerosis, researchers were aware of the potential for drug-induced autoimmunity with Lemtrada.[10] This led to careful consideration—but, as it appears, not by Sanofi—of approaches to prevent or ameliorate this side effect. For example:

- Dr. Alasdair Coles, an individual well known to Sanofi and Genzyme, is currently studying the effect of keratinocyte growth factor to reduce the incidence of autoimmunity after administration of Lemtrada.[11] That study does not appear to be supported by or even sponsored by Genzyme or Sanofi.
- Genzyme employees prior to the merger were actively pursuing research in this area. Thus, a patent application filed in May of 2011 discloses the potential use of the methotrexate after treatment with Lemtrada to prevent secondary autoimmunity. See U.S. Patent Application 61/486,697 (discussing treatment with methotrexate and showing induction of immune tolerance in animal models with clinically relevant doses of Lemtrada).

---

5 In this regard, the recent experiences of Pfizer, Inc. and GlaxoSmithkline with respect to Chantix and Avandia are instructive.

6 J. Jones, et al., "Human Autoimmunity After Lymphocyte Depletion Is Caused By Homeostatic T-Cell Proliferation," 110 PNAS 20200 (Dec. 2013) ("Jones").

7 To the casual observer, there would appear to be a paradox in treating an autoimmune disease with a treatment that can cause autoimmunity. However, the phenomena of autoimmunity secondary to reconstitution of the immune system has been well known for some time. See G. Kroemer, MECHANISM OF IMMUNOLOGICAL SELF-TOLERANCE (1994) 114 (describing autoimmunity after autologous bone marrow reconstitution).

8 Jones at 20201.

9 In this regard, Biogen's and Elan's experience with Tysabri and the stratification of risk of progressive multifocal leukoencephalopathy arising out of the use of natalizumab is instructive.

10 Otton, "Autoimmune Thrombocytopenia After Treatment With CAMPATH 1H In A Patient with Chronic Lymphocytic Leukemia," 106 BRITISH J. HEMAT. 261 (July 1999).

11 Keratinocyte Growth Factor to Prevent Autoimmunity After Alemtuzumab Treatment of Multiple Sclerosis (CAM-THY) NTC0172945, available at www.clinicaltrials.gov.

- Genzyme employees prior to the merger were also actively considering co-administration of Lemtrada with other medications to reduce, among other things, secondary autoimmunity, by reducing the dose of anti-CD52 needed to reach a therapeutic level. Thus, in 2009, Genzyme employees filed a patent application directed to the use of an agent that stimulates neutrophils or NK cells or both with Lemtrada. See U.S. Patent Application No. 61/177922 (stating in part that "[w]e have further discovered that stimulation of neutrophils and/or NK cells allows a clinician to reduce the dose and therefore certain side effects of an anti-CD52 antibody therapy without compromising the efficacy of the therapies").
- Researchers have identified potential markers for risk stratification and treatment responses, as well as provided evidence to support the hypothesis that co-administration of drugs which modulate the IL-21 response may be useful in preventing and ameliorating secondary autoimmunity.[12]

The foregoing list is not exhaustive, but rather is illustrative of the potential approaches that Sanofi should consider. Therefore we request:[13]

1. All documents concerning any clinical development program designed to remove the black box warning for Lemtrada, including, without limitation, any decisions or deliberations by Sanofi concerning the development and/or funding of such a clinical development program.
2. All documents concerning any clinical program designed to develop a treatment for or to prevent reconstitution autoimmunity after Lemtrada treatment, including, without limitation, any decisions or deliberations by Sanofi concerning the development and/or funding of such a clinical program.
3. All documents concerning Sanofi's utilization and/or consideration of the research which led to the filing of U.S. Patent Application 61/486,697 and/or U.S. Patent Application No. 61/177922 in connection with the development, promotion, marketing, and/or sale of Lemtrada.
4. All communications between Sanofi and Dr. Alasdair Coles concerning his above-referenced study.
5. A report, with supporting documentation, summaries (including of associated expenditures and budgets), of all current efforts by Sanofi or Genzyme to directly, or through sponsorship, to undertake clinical development to reduce the incidence of secondary autoimmunity upon the administration of Lemtrada, including, without limitation, the use of biomarkers, co-administration or sequential administration of medications, or the alteration in dosing regimen or route.

---

[12] T Ruck, et al., "LAIN01--Alemtuzumab In Auto-Immune Inflammatory Neurodegeneration: Mechanisms of Action And Neuroprotective Potential," 16 BMC NEUROL. 34 (ar. 2016) (discussing markers and potential additional mechanisms of secondary autoimmunity).

[13] This request is directed at current efforts and should not be taken as a statement that such documents created or actions taken prior to the approval of the BLA for Lemtrada are not relevant to the claims in the Sanofi Action.

II. Initiation of Additional Trials in Multiple Sclerosis

The Phase III clinical trials submitted to the FDA and EMA (CARE-MS I and CARE-MS II) were both in a specific patient population (relapsing multiple sclerosis) and had an active comparator (interferon beta-1a). The Trustee would like to investigate whether Sanofi's Diligent Efforts obligation require it to immediately undertake additional clinical trials in multiple sclerosis.

Therefore we request:

1. All documents concerning the potential or actual initiation of a Phase III clinical trial for Lemtrada in multiple sclerosis, including, without limitation
   a. an open-label trial in this indication;
   b. a trial against interferon beta-1a as comparator;
   c. a trial using a randomized, double-dummy, active-controlled, parallel-group design;
   d. a trial using an adaptive, multi-arm clinical trial design;[14] and/or
   e. a trial in patients with primary progressive multiple sclerosis, either against placebo or against an anti-CD20 antibody in a comparator trial.[15]
2. All documents concerning any consideration by Sanofi of the recent OPERA I and OPERA II studies,[16] including, without limitation, whether such studies suggest that performing a clinical trial, as described above in II.1, would be beneficial from a medical and/or marketing perspective.

III. Development of a Subcutaneous Formulation

Lemtrada is given as an infusion product. There is strong clinical evidence that many of the side effects associated with Lemtrada arise from the infusion process itself. Sanofi recognizes

---

[14] In light of the fact that methodological rigor may well preclude the sole use of active control comparative trials as a basis for deducing efficacy and safety, Lemtrada should be tested in a manner that is more methodologically flexible. The emerging consensus is that such multi-arm trials can provide significant advantages, particularly where, as here, there are multiple potential treatment options. See generally, J. Chataway, "Multi-Arm Trials With Repurposed Drugs in Progressive MS," available at http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2013/ 11/WC500154158 .pdf (describing advantages of adaptive design).

[15] As you aware, Roche has published the results of the ORATORIO study in this patient population. See X Montablan, et. al., "Efficacy and Safety of Ocrelizumab in Primary Progressive Multiple Sclerosis: Results of the Phase III Double-Blind, Placebo-Controlled ORATORIO Study," 86 NEUROLOGY S49.001 (April 2016).

[16] G. Comi, et al. "Effect of Ocrelizumab on Disability Progression in Patients with Relapsing Multiple Sclerosis: Analysis of the Phase III, Double-Blind, Double-Dummy, Interferon Beta-1a-Controlled OPERA I and OPERA II Studies," 86 NEUROLOGY S49.008 (April 2016).

this in its product literature.[17] Sanofi's current approach appears to be to emphasize skilled nursing intervention to prevent infusion-related reactions.[18]

Therefore we request:

1. All documents concerning the potential development of a subcutaneous formulation of Lemtrada,[19] including, without limitation, any clinical trials initiated by Sanofi in connection therewith.

* * *

We suggest a meeting between the Trustee's counsel and Sanofi executives familiar with the foregoing would facilitate satisfaction of the Trustee's inquiry and alleviate burdens on Sanofi in connection with this request. Please advise whether Sanofi will agree to such a meeting and do not hesitate to reach out to me at the above number to discuss the timing of the response to the requests.

Sincerely,

Michael Brenner Weiss

VIA FEDEX AND EMAIL

Sanofi
c/o John Neuwirth, Esq.
Weil, Gotshal & Manges LLP
767 Fifth Avenue
New York, NY 10153-0119

cc. Gavin Wilkinson
Charles A. Gilman, Esq.

---

17 See https://www.lemtrada.com/what-to-expect/lemtrada-patient-videos

18 C. Caon, et al. "Prevention and Management of Infusion-Associated Reactions in the Comparison of Alemtuzumab and Rebif® Efficacy in Multiple Sclerosis (CARE-MS) Program," 17 INT. J. MS CARE 191 (July 2015).

19 Such formulations have been studied by investigators and the Trustee believes the data justifies continued development. C. Tur, et al., "Subcutaneous Alemtuzumab for Multiple Sclerosis," 8 EXPERT REV. CLIN. IMMUNOL. 423 (2012).